Exhibit B Application No.: 08/834,497 Marked-Up Copies of Replacement Paragraphs

Deleted material is bracketed. Added material is underlined. Book titles are underlined here because they were underlined in the Specification as originally filed, and not indicate that the book title has been added.

Please delete the paragraph beginning at page 26, line 4 of the Specification and replace it with the following paragraph:

Mutation analysis was accomplished as follows. Initial searching for the HH mutation in cDNA24 was accomplished through RT-PCR (reverse transcription-polymerase chain reaction, Dracopoli, N. et al. cds. <u>Current Protocols in Human Genetics</u> (J. Wiley & Sons New York (1994)) method. First, from the genotype analysis, homozygous HH patients the ancestral haplotype were identified (see previous sections). First strand cDNAs were synthesized through use of [Superscript] <u>SUPERSCRIPTTM</u> reverse transcriptase (<u>Invitro en Life Technologies, Carlsbad, CA</u>) using polyA+RNA from transformed lymphoblastoid lines from two homozygous ancestral patients (HC9 and HCI4) and those from two unaffected individuals (NY8 and CEPH 11840) as templates.

Please delete the paragraph beginning at page 26, line 33 of the Specification and replace it with the following paragraph:

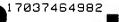
Amplified DNA products (PCR-products) were purified using[gelase] <u>GELASET</u> (Epicentre, <u>Madison</u>, <u>WI</u>), and DNA sequences of these PCR-fragm ents were determine by the dideoxy chain termination method using fluorescently labeled dideoxy nucleotides of an ABI 377 DNA sequencer (<u>Applied Biosystems</u>, <u>Foster City</u>, <u>CA</u>).

Please delete the paragraph beginning at page 32, line 3 of the Specification and replace it with the following paragraph:

cDNA 24 tissue expression was determined by probing polyA+ RNA Northern blass (Clontech, Palo Alto, CA). One major transcript of approximately 4.4 Kb was observed it all of the 16 tissues tested including small intestine and liver.

Please delete the paragraph beginning at page 32, line 6 of the Specification and replace it with the following paragraph:

The genomic region corresponding to cDNA 24 was cloned and sequenced. CDN 24 is comprised of apparently seven exons, covering approximately 11 Kb of sequence. The putative seventh exon is completely non-coding and contains one poly (A)+ addition signal. In the region of the predicted start site of transcription, there are no consensus CAAT or TATA boxes, nor are there any start like βGAP-like sequences recently suggested by Rothenberg and Voland, supra (1996). One CpG island was found to overlap the first exon and extend into the first intron. Within this island are the consensus cis-acting binding signary for the transcription factors Sp1 (2 sites) and AP1 (1 site) ([McVector] MACVECTORT software, Oxford Molecular, San Diego, CA). The lack of any recognizable TATA boxe and the presence of Sp1 and AP2 binding sites is consistent with the low level of transcription associated with the gene.



Please delete the paragraph beginning at page 49, line 30 of the Specification and replace it with the following paragraph:

Depending on the host cell used, transformation is done using standard technique appropriate to such cells (Maniatis et al. supra. (1982); Sambrook et al. supra. (1989); Math. Enzymology supra. (1979, 1983, 1987); U.S. Patent No. 4,399,216; Meth Enzymology supra (1986); Gelvin et al. supra. (1990)). Such techniques include, without limitation, calciur treatment employing calcium chloride for prokaryotes or other cells which contain substated the supra cell wall barriers; infection with Agrobacterium tumefaciens for certain plant cells; calcium phosphate precipitation, DEAE, lipid transfection systems (such as [LipofectinTM] LIPOFECTINTM and [LipofectamineTM] LIPOFECTAMINETM, Invitrogen, Carlsbad CA and electroporation methods for mammalian cells without cell walls, and, microprojectile bombardment for many cells including, plant cells. In addition, DNA may be delivered the viral delivery systems such as retroviruses or the herpes family, adenoviruses, baculoviruses, or semliki forest virus, as appropriate for the species of cell line chosen.

Please delete the paragraph beginning at page 58, line 1 of the Specification and replace it with the following paragraph:

Protein replacement therapy requires that RH protein be administered in an appropriate formulation. The HR protein can be formulated in conventional ways standable the art for the administration of protein substances. Delivery may require packaging in light containing vesicles (such as [LipofectinTM] LIPOFECTINTM or other cationic or anionic or certain surfactant proteins) that facilitate incorporation into the cell membrane. The R protein formulations can be delivered to affected tissues by different methods depending a the affected tissue. For example, iron absorption is initiated in the GI tract. Therefore, delivery by catheter or other means to bypass the stomach would be desirable. In other tissues, IV delivery will be the most direct approach.

Please delete the paragraph beginning at page 65, line 5 of the Specification and replace it with the following paragraph:

In amplification, a solution containing the DNA sample (obtained either directly of through reverse transcription of RNA) is mixed with an aliquot of each of dATP, dCTP, dGTP and dTTP (i.e., Pharmacia LKB Biotechnology, Piscataway, NJ), an aliquot of each the DNA specific PCR primers, an aliquot of Taq polymerase (i.e., Promega, Madison, V and an aliquot of PCR buffer, including MgCl₂ (i.e., Promega) to a final volume. Follow by pre-denaturation (i.e., at 95°C for 7 minutes), PCR is carried out in a DNA thermal cy (i.e., Perkin-Elmer Cetus, Shelton, CT) with repetitive cycles of annealing, extension, and denaturation. As will be appreciated, such steps can be modified to optimize the PCR amplification for any particular reaction, however, exemplary conditions utilized include denaturation at 95°C for 1 minute, annealing at 55°C for 1 minute, and extension at 72°C 4 minutes, respectively, for 30 cycles. Further details of the PCR technique can be found Erlich, "PCR Technology," Stockton Press (1989) and U.S. Patent No. 4,683,202, the disclosure of which is incorporated herein by reference.

Please delete the paragraph beginning at page 73, line 6 of the Specification and replace it with the following paragraph:

The PCR is performed in standard PCR-reaction buffer (e.g., 1X [Geneamp] GENEAMP® reaction buffer from [Perkin Elmer] Applied Biosystems, Foster City, CA with 1.5 mM Mg¹⁻¹) for 35-30 cycles using an annealing temperature of 60°C.

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